C L A I M S

1. A method for inactivating target cells in the presence of T cells by bringing the two types of cells in contact with a superantigen (SAG) in the presence of an immune modulator, characterized in that at least one of the superantigen and the immune modulator is in the form of a conjugate between a "free" superantigen (Sag) and a moiety targeting the conjugate to the target cells.

2. The method of claim 1, characterized in that

   a. the superantigen (SAG) and the immune modulator is used in form of a triple conjugate comprising a superantigen (Sag), a targeting moiety (T) for the target cells and an immune modulator (IM) (T,IM,Sag-conjugate);

   b. the superantigen (SAG) is used in form of a dual conjugate between a superantigen (Sag) and a targeting moiety (T) for the target cells in combination with a dual conjugate between an immune modulator (IM) and a targeting moiety (T') for the target cells (T,Sag-conjugate + T',IM-conjugate);

   c. the superantigen (SAG) is used in form of a dual conjugate between a superantigen (Sag) and a targeting moiety (T) for the target cells and the immune modulator (IM) is used in free form, i.e. not conjugated to a targeting moiety for the target cells (T,Sag-conjugate + IM);

d. the superantigen (SAG) is used in free form (Sag) and the immune modulator is used in conjugate form, i.e. a dual conjugate between the immune modulator and a targeting moiety (Sag + T,IM-conjugate); and

e. the superantigen (SAG) and the immune modulator is used in form of a dual conjugate between a superantigen (Sag) and an immune modulator (IM) (Sag,IM-conjugate).

3. The method according to claim 2, characterized in that alternative a is used.

4. The method according to claim 2, characterized in that alternative b is used, with the possibility that the targeting moiety in the immune modulator conjugate may differ from the targeting moiety in the superantigen conjugate.

5. The method according to claim 2, characterized in that alternative c is used.

6. The method according claim 2 characterized in that alternative e is used and in that IM and T is common, for instance a cytokine receptor, such as IL-2, for targeting the conjugate cells carrying the receptor.

7. The method of anyone of claims 1-6, characterized in that the cells are inactivated in vivo in an individual

suffering from a disease associated with the target cells, for instance a cancer.

8. The method of anyone of claims 1-7, characterized in that the targeting moiety is an antibody, preferably an antigen binding fragment thereof, such as Fab or Fab_2-fragment or a single chain antibody.

9. The method of anyone of claims 1-8, characterized in that the superantigen Sag is modified, for instance by mutation,

a. to have a decreased ability to bind to MHC class II antigen compared to the corresponding wild type superantigen;

b. to have a decreased seroreactivity in human sera compared to the corresponding wild-type superantigen;

c. to have a decreased immunogenicity in human compared to the corresponding wild-type superantigen;

d. to be a chimera between two or more free superantigens.

10. The method of anyone of claims 1-9, characterized in that the superantigen is modified to a reduced MHC class II affinity, for instance by mutation in a codon encoding an amino acid residue of importance for the MHC class II affinity.

11. The method according to anyone of claims 1-10, characterized in that the immune modulator is selected from

a. cytokines, such as IL-2, or

b. chemokines or

c. extracellular parts of lymphocyte surface bound receptors and ligands, for instance the extracellular parts of a B7 molecule, such as CD80 and CD86.

12. The method of anyone of claims 1-11, characterized in that the immune modulator is selected among immune modulators that are capable of potentiating the effects of superantigens in vivo, for instance by counteracting escape of superantigen activated T-cells into anergy.

13. The method of anyone of claims 1-11, characterized in that the immune modulator is the extracellular part of a B7 ligand, such as CD80 or CD86, or a downstream effector of CD28/B7 signaling, such as IL-2.

14. The method of anyone of claims 11-13, characterized in that the immune modulator has been modified, for instance by mutation to show a decreased affinity for its lymphocyte receptor, compared to the corresponding native form.

15. The method according to anyone of claims 1-13, characterized in that the immune modulator is IL-2 or the

extracellular part of CD80 or forms thereof having been modified in accordance with claim 14

16. A superantigen conjugate complying with the formula

$$(T)_x(Sag)_y(IM)_z \qquad \text{Formula I}$$

a. T is a targeting moiety, Sag corresponds to a free superantigen, IM is an immune modulator that is not a superantigen and T, Sag and IM are linked together via organic linkers B that may be different or equal within one and the same conjugate molecule;

b. x, y and z are integers that typically are selected among 0-10, such as 0-5, and represent the number of moieties T, Sag and IM, respectively, in a given conjugate molecule, with the provision that $y > 0$ and also one or both of x and $z > 0$;

17. The superantigen conjugate of claim 16, characterized in that it is a fusion protein in which all x and y and z are integers 1-3, with preference for 1-2, and typical relations between x, y and z being selected among $x = y = z$; $x = y = 0.5z$; $x = 0.5y = 0.5z$; and $x = 0.5y = z$.

18. The superantigen conjugate of claim 16, characterized in that it is a fusion protein expressed as a two chain product.

19. The fusion protein of claim 18 in which the superantigen moiety SAG is fused C-terminally to the targeting moiety

T' and the immune modulator IM is fused C-terminally to the targeting moiety T''.

20. The fusion protein of claim 19 in which T' and T'' are as defined in claim 8, and/or SAG is as defined in anyone of claims 9-10 and/or IM is as defined in anyone of claims 11-15.

21. The fusion protein of claim 20 in which SAG is Staphylococcal enterotoxin A (SEA), T' is the C_H1-domain of C215 Fab fragment, T'' is the light chain of the C215 antibody and IM is interleukin-2.

22. The fusion protein according to claims 19-21 wherein SAG is fused to T' via a flexible hydrophilic amino acid linker B' of 3-11 amino acid residues and IM is fused to T'' via a hydrophilic and neutral or positively charged amino acid linker Q of 10-20 amino acid residues.

23. The fusion protein of claim 22 wherein B' is selected from the group consisting of Gly-Gly-Pro and Pro-Ala-Ser-Gly-Gly-Gly-Gly-Ala-Gly-Gly-Pro (SEQ ID NO: 19) and Q is selected from the group consisting of Gly-Pro-Arg-Gln-Ala-Asn-Glu-Leu-Pro-Gly-Ala-Pro-Ser-Gln-Glu-Glu-Arg (SEQ ID NO: 23), Gly-Pro-Arg-Gln-Ser-Asn-Glu-Thr-Pro-Gly-Ser-Pro-Ser-Gln-Glu-Glu-Arg (SEQ ID NO: 20), Gly-Pro-Arg-Gln-Ala-Lys-Thr-Leu-Pro-Gly-Ala-Pro-Ser-Gln-Thr-Thr-Arg (SEQ ID NO: 21) and Gly-Pro-Thr-Glu-Ala-Asp-Glu-Leu-Pro-Gly-Ala-Pro-Ser-Glu-Glu-Glu-Thr (SEQ ID NO: 22).

24. The superantigen conjugate of claim 16, characterized in that it is a fusion protein, the targeting moiety is absent (x = 0) and y and z are integers 1-3, with preference for 1-2, and preferred relations between x and y being selected among: x = y; x = 0.5y, 0,5x = y; x = 1/3y and 1/3x = y.

25. The superantigen conjugate of claim 16, characterized in having the formula:

$(Sag)_y(IM)_z$ Formula II

in which y = z = 1.

26. The superantigen conjugate according to claims 16, 17, 24 or 25, characterized in that the targeting moiety is as defined in claim 8, and/or the superantigen moiety as defined in anyone of claims 9-10 and/or the immune modulator moiety is as defined in anyone of claims 11-15.

27. A targeted immune modulator, characterized in being a conjugate between a targeting moiety (T''') and a non-superantigen immune modulator (IM''') that has been modified, for instance by mutation, to a decreased affinity to its lymphocyte receptor or to a decreased rate of internalization when becoming bound to its lymphocyte receptor (compared to corresponding native form), said conjugate complying with the formula

$(T''')_x(Sag''')_y(IM''')_z$ Formula V

a. T''' is a targeting moiety, Sag''' corresponds to a free superantigen, IM''' is the modified immune modulator, Sag and IM are linked together via organic linkers B''' that may be different or equal within one and the same conjugate molecule;

b. x, y and z are integers that typically are selected among 0-10, such as 0-5, and represent the number of moieties T''', Sag''' and IM''', respectively, in a given conjugate molecule, with the provision that z > 0 and also one or both of x and y > 0;

28. The targeted immune modulator conjugate of claim 27, characterized in that it is a fusion protein in which all x and y and z are integers 1-3, with preference for 1-2, and typical relations between x, y and z being selected among x = y = z; x = y = 0.5z; x = 0.5y = 0.5z; and x = 0.5y = z.

29. The targeted immune modulator of claim 27, characterized in that it is a fusion protein, the superantigen moiety is absent (y = 0) and x and z are integers 1-3, with preference for 1-2, and preferred relations between x and y being selected among: x = y; x = 0.5y, 0,5x = y; x = 1/3y and 1/3x = y.

30. The targeted immune modulator of claim 29, characterized in that it complies with the formula

$(T''')_y(IM''')_z$

in which y = z = 1.

31. A DNA molecule encoding a superantigen and an immune modulator, such as IL-2, that is not a superantigen.

32. The DNA molecule of claim 31, characterized in that it is in the form of a biscistronic construct in which

a. a first cistron contains a sequence I encoding a polypeptide I comprising an unconjugated superantigen (Sag) that possibly is modified as defined in claims 9-10, and

b. the other cistron contains a sequence II encoding a polypeptide II comprising the immune modulator that possibly is modified as defined in claim 11-15.

33. The DNA molecule of claim 32 characterized in that either or both of sequences I and II are fused to a respective sequence encoding at least a part of an antibody such that polypeptides I and II can associate and form a triple fusion comprising a free superantigen, an immune modulator, and an antibody.

34. The DNA molecule of claim 31, characterized in that the superantigen is a unconjugated superantigen and that the sequence encoding the superantigen is fused to the sequence encoding the immune modulator, possibly via a sequence encoding an oligopeptide linker.